Remarks

Upon entry of this Amendment, claims 1-15 and 19-23 will be pending. Claims 16-18 have been cancelled without prejudice or disclaimer. Claims 2, 7-13 and 19-22 have been withdrawn from consideration by the Examiner. Claims 1, 4 and 6 have been amended to more clearly define the claimed subject matter. New claim 23 has been added as indicated above. Support for the amendments and new claim can be found throughout the specification as filed. Applicants assert that no new matter has been added by way of these amendments.

Applicants respectfully point out that in the August 22, 2006 Office Action, claims 1-22 are pending and subject to Election/Restriction, not claims 1-20 as indicated therein.

Applicants also note that documents AS22 through AR23, cited on page 7 of the form PTO/SB/08B filed October 6, 2005 were not initialed in the August 22, 2006 Office Action. Applicants ask that these documents be considered by the Examiner and that page 7 of Applicants' form PTO/SB/08B with the Examiner's initials be returned to Applicants with the next Office Communication.

Claim Objections

The drawings are objected to because Figure 2 is too dark and the writing is not legible. This Amendment is accompanied by replacement drawing sheets 1-10 and an annotated drawing sheet outlining the changes made to Figure 2, in accordance with the objection. As the Examiner's objection is now obviated, Applicants respectfully request that the objection be withdrawn.

Claims 1 and 16-18 are objected to as containing non-elected subject matter pertaining to SEQ ID NOs: 3 and 4. With this Amendment, claim 1 has been amended and claims 16-18 have been cancelled. As the Examiner's objection is now obviated, Applicants respectfully request that the objection be withdrawn.

Claim 4 is objected to because it contains an improper Markush group. The Office Action states that, "the host cell and vector do not share substantial structural features to be included in the same Markush group." With this Amendment, the subject matter of claim 4 has been amended and new claim 23 has been added. As the Examiner's objection is now obviated, Applicants respectfully request that the objection be withdrawn.

Sequence Rules Compliance

Figure 2A is objected to because it contains sequences but no corresponding "SEQ ID NO," as required by 37 C.F.R. 1.821-1.825. With this Amendment, Figure 2A has been replaced with Replacement Sheet Figure 2A, which includes the appropriate SEQ ID NOs. Also, Applicants note that amino acid sequence "KIAA0923" of Figure 2A is not contained in the original Sequence Listing filed for the present application. Applicant has corrected this oversight and has included amino acid sequence "KIAA0923" cited as SEQ ID NO: 9, to the Sequence Listing accompanying this Amendment. As the Examiner's objection is now obviated, Applicants respectfully request that the objection be withdrawn.

Right of Priority

The Office Action states that Applicant has claimed foreign priority to Japan 2002-284263 but has not provided a translation of the foreign priority document. Accompanying this Amendment, Applicant provides an English translation of foreign priority document Japan 2002-284263. As the Examiner's objection is now obviated, Applicants respectfully request that the objection be withdrawn.

Claim Rejections – 35 U.S.C. § 101

Claims 1, 4, 6 and 14-18 are rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter. The Examiner states that the claims do not recite "an isolated and purified" when referring to polynucleotides and host cells carrying polynucleotides.

With this Amendment, Applicants have cancelled claims 16-18 and have amended claims 1, 4 and 6 to recite the phrase, "An isolated and purified." Claims 14-15 depend from claim 1, and thereby incorporate the phrase. As the Examiner's rejection is now obviated, Applicants respectfully request that the objection be withdrawn. Applicants submit that amended claims 1, 4 and 6 and claims dependent thereon comply with U.S.C. § 101 and, therefore, respectfully request that the Examiner withdraw this rejection

Claim Rejections – 35 U.S.C. § 112, second paragraph

Claims 1, 3-6 and 14-18 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner states that Claims 1(d) and 6 are indefinite because "stringent conditions" for hybridization are not specified; claim 1(c) because the use of "in which the amino acids are substituted, deleted, inserted and/or added" is indefinite; claim 1(b) because it is not clear if Applicant is claiming a polynucleotide comprising any coding region of the nucleotide sequence of SEQ ID NO: 1 or claiming a polynucleotide comprising the complete coding region which encodes the polynucleotide of SEQ ID NO: 2; Claim 1(b) is also allegedly not clear in regards to what "coding region" refers to; claim 4 because it is not clear what is meant by host cell "carrying;" and claims 3, 5 and 14-18 are rejected for depending on an indefinite base claim.

With this Amendment, claims 16-18 are cancelled and claims 1, 4 and 6 have been amended to further clarify the invention. Claim 1(d) has been deleted and claim 6 has been amended to remove the phrase "which specifically hybridizes under highly stringent conditions to the polynucleotide of claim 1." Claim 1(c) has been amended to remove the phrase "substituted, deleted, inserted and/or added." Claim 1(b) has been amended to remove the phrase "a coding region" and to add a specific reference to the nucleotide sequence "corresponding to position 80 to 1924." Finally, claim 4 has been amended to remove the phrase "host cell carrying" and add "host cell transformed with,"

in order to further clarify the invention. Claims 3, 5 and 14-15 depend from amended claim 1.

Applicants submit that amended claims 1, 4 and 6 and claims dependent thereon comply with 35 U.S.C. § 112, second paragraph and, therefore, respectfully request that the Examiner withdraw this rejection.

Claim Rejections – 35 U.S.C. § 112, first paragraph

Enablement

Claims 1, 3-6 and 14-18 are rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not provide enablement for the claimed variants. The Examiner states that the specification, while being enabling for an isolated polynucleotide encoding a polypeptide which binds afadin, α-actinin-1 or α-actinin-2, a vector comprising the polynucleotide and host cell comprising said vector, and using said host cell to produce the claimed polynucleotide; does not reasonably provide enablement for other polynucleotides.

With this Amendment, claims 16-18 are cancelled and claims 1, 4 and 6 have been amended to further clarify the invention.

Claim 1 has been amended to recite "a polynucleotide comprising the nucleotide sequence with at least 95% homology to the nucleotide sequence corresponding to position 80 to 1924 in SEQ ID NO: 1 which have the binding activity to afadin and/or actinin." Applicants believe that this places claim 1 and the claims dependent thereon in condition for allowance.

Applicants respectfully direct the attention of the Examiner to the enablement decision tree set forth in the Examiner's Training Materials (found at http://www.uspto.gov/web/offices/pac/dapp/1pecba.htm#7) under "Training Materials For Examining Patent Applications With Respect To 35 U.S.C. § 112, First Paragraph - Enablement Chemical/Biotechnical Applications." A courtesy copy of this document is attached hereto as Exhibit A. The decision tree first asks the question "Does the

specification teach how to make and use at least one embodiment encompassed by the claims as a whole without undue experimentation?" A note to the question states that "if there is a working example, the answer cannot be 'No'." In the present application, the Applicants not only provide general guidance as to how to make and use embodiments of the claimed invention, but also describe representative species that fall within the scope of the claimed invention (i.e. SEQ ID NO: 1). Accordingly, the answer to the question is necessarily "Yes."

The second question in the enablement decision tree is "Are the enabled embodiments representative of the full scope of the claim?" As discussed above, the USPTO has deemed a single disclosed species to be representative of the claimed genus of homologs and sequence variants encompassed by the claims. Specifically, the high degree of sequence identity yields structurally similar nucleotides; therefore a person of skill in the art would not expect substantial variation among species within the genus. Accordingly, as Applicants have disclosed a representative species (i.e. SEQ ID NO: 1), the answer to this second question is necessarily "Yes."

The Examiner suggests that without specific guidance as to which amino acids may be mutated, the experimentation left to those skilled in the art is undue. Applicants, however, respectfully point out that it is important to remember that the test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, provided it is merely routine. See *In re Wan*ds, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In *Wands*, it was found that "trial and error testing" testing needed to identify regions of the protein that can tolerate mutation is within the parameters of routing experimentation and optimization.

Applicants submit that amended claims 1, 4 and 6 and claims dependent thereon comply with 35 U.S.C. § 112, first paragraph and, therefore, respectfully request that the Examiner withdraw this rejection.

Written Description

Claims 1, 3-6, and 15-18 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. The Examiner states that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention.

With this Amendment, claims 16-18 are cancelled and claims 1, 4 and 6 have been amended to further clarify the invention.

Claim 1(d) has been deleted and claim 6 has been amended to remove the phrase "which specifically hybridizes under highly stringent conditions to the polynucleotide of claim 1." Claim 1(c) has been amended to remove the phrase "substituted, deleted, inserted and/or added." Claim 1(b) has been amended to remove the phrase "a coding region" and add a specific reference to the nucleotide sequence "corresponding to position 80 to 1924." Finally, claim 4 has been amended to remove the phrase "host cell carrying" and add the phrase "host cell transformed with," in order to further clarify the invention. Claims 3, 5 and 15 depend from amended claim 1.

Regarding amended claim 1(c), Applicants have limited the claim to a polynucleotide comprising the nucleotide sequence with at least 95% homology to the nucleotide sequence corresponding to position 80 to 1924 in SEQ ID NO: 1, which have the binding activity to afadin and/or actinin. USPTO guidelines and policy supports patentability of this type of claim in regards to the written description analysis as set forth in the "Revised Interim Written Description Guidelines," published January 5, 2001, in particular the Training Materials accompanying the same (See http://www.uspto.gov/web/menu/written.pdf). A courtesy copy of the Training Materials is attached hereto as Exhibit B. Specifically, Example 14 of the Training Materials analyzes a claim directed to variants of a protein that are at least 95% identical to a particular disclosed sequence and that have a particularly specified activity.

The Training Materials conclude that "the genus of proteins that must be variants . . . does not have substantial variation since all the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence." Thus, "the single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants . . . which are capable of the specified catalytic activity." Accordingly, "one of skill in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus" (i.e. the example claim meets the written description requirement of 35 U.S.C. § 112, first paragraph). See Training Materials, pages 53-55.

Amended claim 1 is analogous to the claim from Example 14 of the Training Materials in that it is directed to an isolated nucleic acid encoding a protein having at least 95% identity to a reference sequence and having a specifically identified function. As discussed above, since the species are defined both in terms of specific structure and specific function, the genus of nucleotides encompassed by the claim will not have substantial variation. Thus, it follows that, since the genus is not widely variable, a single species is sufficient to demonstrate possession. Furthermore, Applicants' specification sets forth assays for preparing and identifying such variants capable of performing the specified function. See, for example, page 20 lines 21-24; page 44, Example 4 (identification of afadin-binding protein); page 20, line 26, to page 21, line 24; page 24 lines 16-21 (introducing mutations); and page 21, line 25, to page 22, line 3 (determining percent identity). Accordingly, the instant specification provides an adequate written description of the genus of sequence variants encompassed by claim 1(c), so as to convey with reasonable clarity to those skilled in the art that, as of the filing date sought, Applicants were in possession of the invention now claimed.

Applicants submit that amended claims 1, 4 and 6 and claims dependent thereon comply with 35 U.S.C. § 112, first paragraph and, therefore, respectfully request that the Examiner withdraw this rejection.

Claim Rejections – 35 U.S.C. § 102

Claims 1, 3, 4, 6 and 15-18 are rejected under 35 U.S.C § 102(b), as being allegedly anticipated by The RIKEN Genome Exploration Research Group Phase II Team and the FANTOM Consortium. The Examiner states that the reference discloses a polynucleotide which has 99.4% query match and 99.9% identity to the polynucleotide of SEQ ID NO: 1. The Examiner also states that a vector comprising said polynucleotide and cell comprising said vector are disclosed.

Claims 1, 3, 4, 6 and 15-18 are rejected under 35 U.S.C § 102(b), as being allegedly anticipated by Carninci *et al.* The Examiner states that the reference discloses a polynucleotide which has 99.4% query match and 99.9% identity to the polynucleotide of SEQ ID NO: 1. The Examiner also states that a vector comprising said polynucleotide and cell comprising said vector are disclosed.

Claims 1, 3, 4, 6 and 15-18 are rejected under 35 U.S.C § 102(e), as being allegedly anticipated by Takao Isogai *et al.* (US Patent No. 6,943,241). The Examiner states that the reference discloses a polynucleotide which has 46.8% query match and 77.2% identity to the polynucleotide of SEQ ID NO: 1. The Examiner also states that a vector comprising said polynucleotide and cell comprising said vector are disclosed.

Claims 1, 3, 4-6 and 15-18 are rejected under 35 U.S.C § 102(b), as being allegedly anticipated by Helix Research Institute (European Patent No. 1,074,617). The Examiner states that the reference discloses a polynucleotide which has a 46.8% query match and a 79.7% identity to the polynucleotide of SEQ ID NO: 1. The Examiner also states that a vector comprising said polynucleotide and cell comprising said vector are disclosed.

Claims 1, 3, 4, 6 and 14-18 are rejected under 35 U.S.C § 102(a), as being allegedly anticipated by Mammalian Gene Collection Program Team. The Examiner states that the reference discloses a polynucleotide which has a 99.9% query match and a 99.9% identity to the polynucleotide of SEQ ID NO: 1. The Examiner also states that a vector comprising said polynucleotide and cell comprising said vector are disclosed.

Claims 1, 3-6 and 15 are rejected under 35 U.S.C § 102(b), as being allegedly anticipated by Hayashi *et al.* (US Patent No. 5,739,008). The Examiner states that the reference discloses a polynucleotide encoding actin, vector comprising said polynucleotide, cell comprising said vector and a method of using the cell to produce the encoded polypeptide. The Examiner also states that actin inherently binds afadin.

With this Amendment, claims 16-18 are cancelled and claims 1, 4 and 6 have been amended to further clarify the invention.

Amended claim 1(c) recites a polynucleotide comprising the nucleotide sequence with at least 95% homology to the nucleotide sequence corresponding to position 80 to 1924 in SEQ ID NO: 1 which have the binding activity to afadin and/or actinin. The references cited above disclose genome sequences which have 99.9% identity to the polynucleotide of SEQ ID NO: 1, however, these references do not disclose the specific nucleotide sequence in the corresponding genome sequences (i.e. position 80 to 1924 in SEQ ID NO: 1). Therefore, the cited references do not disclose each and every element recited in claim 1 of the present invention.

Based on the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the rejections under 35 U.S.C. § 102.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Annotated sheet

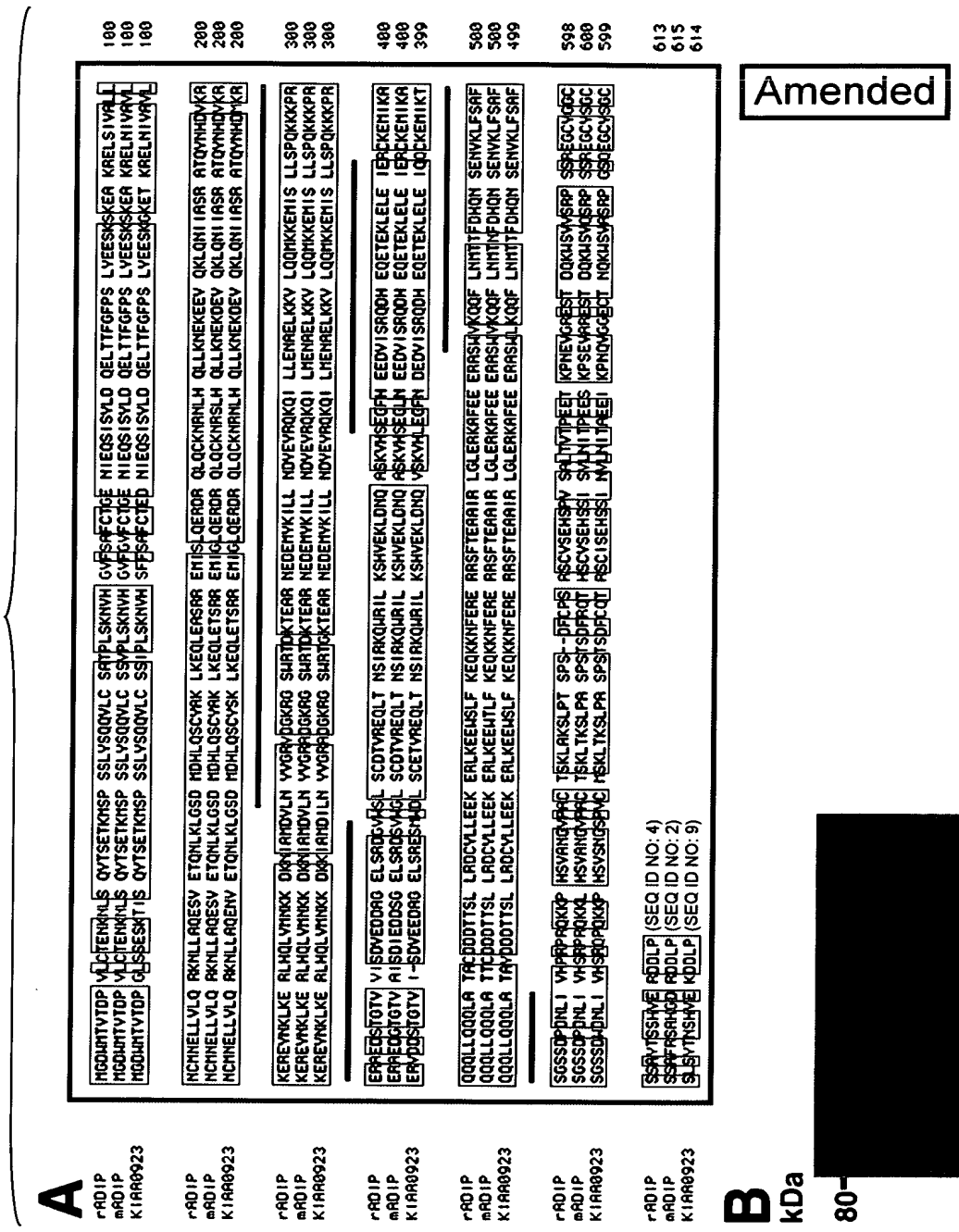

FIG. 2